

## REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

### **Pending Claims**

Prior to this Amendment, Claims 1-3 were pending. Applicants assume that Claim 3 is allowable if rewritten in an independent form because the Examiner did not reject to Claim 3.

Claim 1 was amended. New Claims 9-41 are added by this Amendment.

### **Incorporation by reference**

Consistent with the guidelines in MPEP §608(p), Applicants are adding material from WO 98/51325 to the specification. WO 98/51325 is a published application that was incorporated by reference into the present application as can be seen from the following 2 excerpts from the present application:

As disclosed and claimed in WO 98/51325, which reference is hereby incorporated by reference in its entirety, we have identified random peptides and their fragments, motifs, derivatives or peptidomimetics thereof which are capable of specific binding to GIT receptors such as the D2H, hSI, HPT1 and hPEPT1 receptors (hereinafter "GIT targeting agents"). (From page 2, lines 26-29 to page 3, lines 1-2).

Additional GIT targeting agents are disclosed throughout the above referenced WO 98/51325 (From page 6, line 1-2).

Material incorporated by reference from WO 98/51325 is summarized in the following Table 1:

TABLE 1

<b>Material</b>	<b>Location in WO 98/51325</b>	<b>Insert position in specification of present application</b>	<b>Claims in which Material appears in application</b>
Information on GIT receptors	page 45 line 25 to page 46, line 37	Page 6, after line 2	1-41
Sequences of 55 receptor-binding peptides identified from a phage library (SEQ ID NOS: 17-71)	page 54, lines 5 to page 55, lines 37	Immediately following above insert	10, 11, 12, 13, 19, 20, 21, 22, 28, 29, 30, 31, 37, 38, 39, and 40
Sequences of 13 binding motifs (SEQ ID NOS 72-84)	Claims 6, 10, 14, 18-20 Sequence Listing SEQ ID NOS: 253-265	Sequence Listing	14, 23, 32, and 41
Sequences of 4 GIT receptors (SEQ ID NOS: 13-16)	Sequence Listing SEQ ID NOS:181, 179, 178, and 176	Sequence Listing	9, 10, 11, 12, 13, 14, 18, 19, 20, 21, 22, 23, 27, 28, 29, 30, 31, 36, 37, 38, 39, and 40.

## **Changes made in text incorporated by reference**

Applicants have incorporated text from page 45, line 25 to page 46, line 36 of WO 98/51325. The following changes were made:

- 1) Moved the title of the table, " TARGET BINDING PHAGE INSERT SEQUENCES" to become the header to the right column : --TARGET BINDING PHAGE INSERT SEQUENCE--
- 2) Changed the SEQ ID NOS from 1-55 to 17-71.
- 3) Changed the SEQ ID NOS from 176,178,179, and 181 to 16, 15, 14, and 13 respectively.
- 4) Changed the SEQ ID NOS from 253-265 to 72-84.
- 5) In the section titled "6.2. Cloning of Extracellular Domain of Selected Receptor Site" removed "6.2." from the title and added a section titled "SEQ ID NOS."

## **Support for Amendments**

The following examples of support for any given claim amendment are intended to be illustrative, not exhaustive.

### Support for amendments to Claim 1

Support for amendments to Claim 1 can be found in the application as filed starting on Page 2, line 26 through Page 4 line 4 wherein GIT targeting agents are defined and further on Page 5, lines 19-26 through Page 6 line 2.

### Support for new Claims 9-41

New Claims 9-41 are supported generally by the application as filed and specifically, by the material incorporated by this Amendment (See Table 1 above).

New Claims 24-41 parallel claims 1-3 and 9-23, with the difference that independent

Claim 24 has different language than Claim 1 has.

Support for newly added amino acid sequences

The SEQ ID NOS of newly added sequences incorporated by reference from WO 98/51325 are presented in Table 2 below together with their corresponding SEQ ID NOS from WO 98/51325.

TABLE 2

SEQ ID NOS in present application	SEQ ID NOS in WO 98/51325	Nature of peptide/protein
17-71	1-55	Targeting agents
72-84	253-265	Targeting agents
16	176	hPEPT1 receptor
15	178	HPT1 receptor
14	179	hSI receptor
13	181	D2H receptor

**Appendix to this Amendment**

Applicants have attached an Appendix with copies of those pages from the WO 98/51325 that have the material that was incorporated via the present Amendment into the present application.

**Sequence Listing**

A "Transmittal of Sequence Listing and Related Amendment" is being co-submitted with this Amendment in view of the additional sequences added by this Amendment.

**Response to Rejections in Office Action of July 5, 2002.**

**Rejection of Claims 1 and 2 under 35 U.S.C. 112, first paragraph (Page 2 of the Office Action)**

The Examiner has rejected Claims 1 and 2 under 35 U.S.C. §112, first paragraph, as being indefinite for failing to particularly point out and claim the subject matter of the invention, specifically for failing to define "GIT." In response, Applicants have defined GIT.

**Rejection of Claims 1 and 2 under 35 U.S.C. 102(b) (Page 2 of the Office Action)**

The Examiner has rejected Claims 1 and 2 under 35 U.S.C. §102(b) as being anticipated by two references by Lobie et al. Applicants respectfully traverse this rejection.

Lobie at al (1993) teaches producing an antibody to the rabbit mammary gland prolactin receptor. Lobie at al (1990) teaches producing an antibody to the growth hormone receptor.

Neither of the two Lobie et al references teach an antibody against a protein which binds to a receptor (such as a GIT transport receptor). Therefore, neither Lobie et al reference anticipates Applicants' claimed inventions.

In view of the foregoing remarks, it is respectfully submitted that all of the claims now pending in this application are allowable.

Respectfully submitted,  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Amended) An antibody or antibody fragment specific to a domain of a gastro-intestinal tract (GIT) targeting agent, said targeting agent comprising a protein that specifically binds to a GIT receptor.

**Appendix with pages from WO 98/512325**

The following pages are attached:

45-46

54-55

179-180

184-189

192-194

234-237

Material incorporated by reference into the present application is marked by a vertical black line in the right margins.

form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient.

The Therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts 5 include those formed with free amino groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with free carboxyl groups such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, 10 triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the Therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the 15 disorder or condition, and can be determined by standard clinical techniques. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the 20 seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances.

## 6. EXAMPLES

### 25 6.1. Selection of GIT Receptor Targets

The HPT1, hPEPT1, D2H, and hSI receptors were selected for cloning as GIT receptor targets based on several criteria, including: (1) expression on surface of epithelial cells in gastro-intestinal tract (GIT); (2) expression along 30 the length of small intestine (HPT1, hPEPT1, D2H); (3) expression locally at high concentration (hSI); (4) large putative extracellular domains facing into the lumen of the GIT; and (5) extracellular domains that permit easy access and bioadhesion by targeting particles.

35 The four recombinant receptor sites screened with the peptide libraries additionally have the following characteristics:

	<u>Receptor</u>	<u>Characteristics</u>
	D2H	Transport of neutral/basic amino acids; a transport activating protein for a range of amino acid translocases
5	hSI	Metabolism of sucrose and other sugars; represents 9% of brush border membrane protein in Jejunum
	HPT1	di/tri peptide transporter or facilitator of peptide transport
	hPEPT1	di/tri peptide transporter
10	Figures 1-4 (SEQ ID NOS:176, 178, 179, and 181, respectively) show the predicted amino acid sequences for hPEPT1, HPT1, hSI and D2H, respectively.	

15           6.2. Cloning of Extracellular Domain of  
Selected Receptor Site  
The following receptor domains were cloned and expressed as His-tag fusion proteins by standard techniques:

	<u>Receptor</u>	<u>Domain (amino acid residues)</u>
20	hPEPT1 <sup>a</sup>	391-571
	HPT1 <sup>b</sup>	29-273
	hSI <sup>c</sup>	272-667
	D2H <sup>d</sup>	387-685

25           <sup>a</sup> Liang et al., 1995, J. Biol. Chem. 270:6456-6463  
<sup>b</sup> Dantzig et al., 1994, Association of Intestinal Peptide Transport with a Protein Related to the Cadherin Superfamily  
<sup>c</sup> Chantret et al., Biochem. J. 285:915-923  
<sup>d</sup> Bertran et al., J. Biol. Chem. 268:14842-14949

30           The receptor proteins were expressed as His-tag fusion proteins and affinity purified under denaturing conditions, using urea or guanidine HCl, utilizing the pET His-tag metal chelate affinity for Ni-NTA Agarose (Hochuli, E., Purification of recombinant proteins with metal chelate adsorbent, Genetic Engineering, Principles and Methods (J.K. Setlow, ed.), Plenum Press, NY, Vol. 12 (1990), pp. 87-98).  
35

plates were treated with PBS containing 0.1% phenylhydrazine for one hour at 37°C followed by two PBS washes and blocking for one hour with 0.5%BSA-PBS. The standard ELISA procedure was followed at this point.

5 Phage which showed specificity to a GIT receptor was further characterized by ELISA on a variety of recombinant proteins. Phage which continued to exhibit GIT receptor specificity was sequenced.

10

Table 7

TARGET BINDING PHAGE INSERT SEQUENCES:

<u>hSI</u>	<u>ID. NO.</u>	<u>SEQ.</u>
S15	1	RSGAYESPDRGGGRSYVGGGGCGNIGRKHNLWGLRTASPACWD
S21	2	SPRSFWPVVSRRHESFGISNYLGCGYRTCISGTMTKSSPIYPRHS
15 S22	3	SSSDWGGVPGKVVRFKGRGCCISITSVLTGKPNCPEPKAA
SNi10	4	RVGQCTDSDVRRPWARSCHAQGCGAGTRNSHGCITRPLRQASAH
SNi28	5	SHSGGMNRAYGDVFRELRDRWNATSHTRPTPQLPRGPN
SNi34	6	SPCGGSWGRFMQGGLFGGRTDGCAHNRNTSASLEPPSSDY
SNi38	7	RGAADQRRGWSENLGLPRVGWDAIAHNSYTFTSRRPRPP
20 SNi45	8	SGGEVSSWGRVNNDLCARVSWTGCCTARSARTDNKGFLPKHSSLR
SNiAX2	9	SDSDGDHYGLRGGVRCSLDRGCGLALSTVHAGPPSFYPKLSSP
SNiAX4	10	RSLGNYGVTGTVDTVLPMPGHANHLGVSSASSSDPPRR
SNiAX6	11	RTTTAKGCLLGSFGVLSGCSFTPTSPPPHLGYPPHSVN
SNiAX8	12	SPKLSSVGVMTKVTELPTEGPNAISIPISATLGPRNPLR
25		
		<u>D2H</u>
DAB3	13	RWCGAELCNSVTKKFRPGWRDHANPSTHHRTPPPSQSSP
DAB7	14	RWCGADDPCGASRWGGNSLFGCGLRCSAAQSTPSGRIHSTSTS
DAB10	15	SKSGEGGDSSRGETGWARVRSHAMTAGRFRWYNQLPSDR
30 DAB18	16	RSSANNCEWKSDWMRRACIARYANSSGPARAVDTKAAP
DAB24	17	SKWSWSSRWGSPQDKVEKTRAGCGGSPSSTNCHPYTFAPPPQAG
DAB30	18	SGFWFCSRGLWDGENRKSVRSGCGFRGSSAQGPCPVTPATIDKH
DAX15	19	SESGRCRSVSRWMTTWQTQKGGCGSVSRGSPLDPSHQTHATT
DAX23	20	REWRFAGPPLDLWAGPSLPSFNASSHPRALRTYWSQRPR
35 DAX24	21	RMEDIKNSGWRDSCRWGDLRPGCGSRQWYPSNMRSSRDYPAGGH
DAX27	22	SHPWYRHWNHGDFSGSGQSRHTPPESPHPGRPNATI

	DCX8	23	RYKHDIGCDAGVDKKSSSVRGCGAHSSPPRAGRGPRTMVSRL
	DCX11	24	SQGSKQCMQYRTGRLTVGSEYGCGMNPARHATPAYPARLLPRYR
	DCX26	25	SGRTTSEISGLWGWDGDRSGYWGNTLRPNYIPYRQATNRHRYT
	DCX33	26	RWNWTVLPATGGHYWTRSTDYHAINNHRPSIPHQHPTPI
5	DCX36	27	SWSSWNWSSKTTRLGDRATREGCGPSQSDGCPYNGRLTTVKPRT
	DCX39	28	SGSLNAWQPRSWVGGAFRSHANNNLNPKPTMVTRHPT
	DCX42	29	RYSGLSPRDNGPACSQEATLEGCGAQRLMSTRRKGRNSRPGWTL
	DCX45	30	SVGNDKTSRPVSFYGRVSDLWNASLMPKRTPSSKRHDDG

10 hPEPT1

	PAX9	31	RWPSSVGYKGNGSDTIDVHSNDASTKRSЛИNHRRPLFP
	PAX14	32	RTFENDGLGVGRSIQKKSDRWYASHNIRSHFASMSPAGEK
	PAX15	33	SYCRVKGGEGGGHTDSNLARSGCGKVARTSRLQHINPRATPPSR
	PAX16	34	SWTRWGKHTHGGFVNKSPPGKNATSPYTDAQLPSDQGPP
15	PAX17	35	SQVDSFRNSFRWYEPSRALCHGCGKRDSTTRIHNPSDSYPTR
	PAX18	36	SFLRFQSPRFEDYSRTISRLRNATNPSNVSDAHNNRALA
	PAX35	37	RSITDGGINEVDLSSVSNVLENANSHRAYRKHRPTLKRP
	PAX38	38	SSKVSSPRDPTVPRKGGNVDYGCGRSSARMPTSALSSITKCYT
	PAX40	39	RASTQGGRGVAPEFGASVLGRGCGSATYYTNSTSCKDAMGHNYS
20	PAX43	40	RWCEKHKFTAARCSAGAGFERDASRPPQPAHRDNTNRNA
	PAX45	41	SFQVYPDHGLERHALDGTGPLYAMPGRWIRARPQNDRDQ
	PAX46	42	SRCTDNEQCPDTGTRSRSVSNARYFSSRLLKTHAPHRP
	P31	43	SARDSGPAEDGSRAVRLNGVENANTRKSSRSNPRGRRHP
	P90	44	SSADAEKCAGSLLWWGRQNNNSCGSPTKKHLKHRNRSQTSSSH
25	5PAX3	45	RPKNVADAYSSQDGAAAEETSHASNAARKSPHKPLRRP
	5PAX5	46	RGSTGTAGGERSGVLNLHTRDNASGSGFKPWYPSNRGHK
	5PAX7	47	RWGWERSPSDMDLGARRYATRTHRAPPRLKAPLP
	5PAX12	48	RGWKCEGSQAAYGDKDIGRSRGCGSITKNNTNHAHPHGVAVAKI

30 HPT-1

	HAX9	49	SREEANWDGYKREMSHRSRFWDATHLSRPRRPANGDPN
	HAX35	50	EWYSWKRSSKSTGLGDTATREGCGPSQSDGCPYNGRLTTVKPRK
	HAX40	51	REFAERRLWGCDLWRDLAEGCGPTPSNRAVKHRKPRPRSPAL
	HAX42	52	SDHALGTNLRSDNAKEPGDYNCCGNNSTGRKFVNRRPSAIPT
35	HCA3	53	RHISEYSFANSHLMGGESKRKGCGINGSFSPTCPRSPTPAFRRT
	H40	54	SRESGMWGSWRGHRLNSTGGNANMNASLPPDPVVSTP
	PAX2	55	STPPSREAYSRPYSVDSDSDTNAKHSSHNRRLRTRSRPN

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

**(C) STRANDEDNESS:**

(ii) MOLECULE TYPE: peptide

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

Arg Arg Leu Arg Thr Arg Ser Arg Pro Asn  
1 5 10

(2) INFORMATION FOR SEQ ID NO:176:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 708 amino acids

(B) TYPE: amino acid

**(C) STRANDEDNESS :**

#### (iii) MOLECULAR TYPE: peptido-

(vi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

15 Met Gly Met Ser Lys Ser His Ser Phe Phe Gly Tyr Pro Leu Ser Ile  
       1                             5                             10                             15  
 Phe Phe Ile Val Val Asn Glu Phe Cys Glu Arg Phe Ser Tyr Tyr Gly  
       20                             25                             30  
 Met Arg Ala Ile Leu Ile Leu Tyr Phe Thr Asn Phe Ile Ser Trp Asp  
       35                             40                             45  
 Asp Asn Leu Ser Thr Ala Ile Tyr His Thr Phe Val Ala Leu Cys Tyr  
       50                             55                             60  
 Leu Thr Pro Ile Leu Gly Ala Leu Ile Ala Asp Ser Trp Leu Gly Lys  
       65                             70                             75                             80  
 Phe Lys Thr Ile Val Ser Leu Ser Ile Val Tyr Thr Ile Gly Gln Ala  
       85                             90                             95  
 Val Thr Ser Val Ser Ser Ile Asn Asp Leu Thr Asp His Asn His Asp  
       100                             105                             110  
 Gly Thr Pro Asp Ser Leu Pro Val His Val Val Leu Ser Leu Ile Gly  
       115                             120                             125  
 Leu Ala Leu Ile Ala Leu Gly Thr Gly Gly Ile Lys Pro Cys Val Ser  
       130                             135                             140  
 20 Ala Phe Gly Gly Asp Gln Phe Glu Glu Gly Gln Glu Lys Gln Arg Asn  
       145                             150                             155                             160  
 Arg Phe Phe Ser Ile Phe Tyr Leu Ala Ile Asn Ala Gly Ser Leu Leu  
       165                             170                             175  
 Ser Thr Ile Ile Thr Pro Met Leu Arg Val Gln Gln Cys Gly Ile His  
       180                             185                             190  
 Ser Lys Gln Ala Cys Tyr Pro Leu Ala Phe Gly Val Pro Ala Ala Leu  
       195                             200                             205  
 Met Ala Val Ala Leu Ile Val Phe Val Leu Gly Ser Gly Met Tyr Lys  
       210                             215                             220  
 25 Lys Phe Lys Pro Gln Gly Asn Ile Met Gly Lys Val Ala Lys Cys Ile  
       225                             230                             235                             240  
 Gly Phe Ala Ile Lys Asn Arg Phe Arg His Arg Ser Lys Ala Phe Pro  
       245                             250                             255  
 Lys Arg Glu His Trp Leu Asp Trp Ala Lys Glu Lys Tyr Asp Glu Arg  
       260                             265                             270  
 Leu Ile Ser Gln Ile Lys Met Val Thr Arg Val Met Phe Leu Tyr Ile  
       275                             280                             285  
 30 Pro Leu Pro Met Phe Trp Ala Leu Phe Asp Gln Gln Gly Ser Arg Trp  
       290                             295                             300  
 Thr Leu Gln Ala Thr Thr Met Ser Gly Lys Ile Gly Ala Leu Glu Ile  
       305                             310                             315                             320  
 Gln Pro Asp Gln Met Gln Thr Val Asn Ala Ile Leu Ile Val Ile Met

	325	330	335
	Val Pro Ile Phe Asp Ala Val Leu Tyr	Pro Leu Ile Ala Lys	Cys Gly
	340	345	350
	Phe Asn Phe Thr Ser Leu Lys Lys Met Ala Val Gly	Met Val Leu Ala	
	355	360	365
	Ser Met Ala Phe Val Val Ala Ala Ile Val Gln Val	Glu Ile Asp Lys	
	370	375	380
5	Thr Leu Pro Val Phe Pro Lys Gly Asn Glu Val Gln Ile Lys Val Leu		
	385	390	395
	Asn Ile Gly Asn Asn Thr Met Asn Ile Ser Leu Pro Gly Glu Met Val		
	405	410	415
	Thr Leu Gly Pro Met Ser Gln Thr Asn Ala Phe Met Thr Phe Asp Val		
	420	425	430
	Asn Lys Leu Thr Arg Ile Asn Ile Ser Ser Pro Gly Ser Pro Val Thr		
	435	440	445
	Ala Val Thr Asp Asp Phe Lys Gln Gly Gln Arg His Thr Leu Leu Val		
10	450	455	460
	Trp Ala Pro Asn His Tyr Gln Val Val Lys Asp Gly Leu Asn Gln Lys		
	465	470	475
	Pro Glu Lys Gly Glu Asn Gly Ile Arg Phe Val Asn Thr Phe Asn Glu		
	485	490	495
	Leu Ile Thr Ile Thr Met Ser Gly Lys Val Tyr Ala Asn Ile Ser Ser		
	500	505	510
	Tyr Asn Ala Ser Thr Tyr Gln Phe Phe Pro Ser Gly Ile Lys Gly Phe		
	515	520	525
15	Thr Ile Ser Ser Thr Glu Ile Pro Pro Gln Cys Gln Pro Asn Phe Asn		
	530	535	540
	Thr Phe Tyr Leu Glu Phe Gly Ser Ala Tyr Thr Tyr Ile Val Gln Arg		
	545	550	555
	Lys Asn Asp Ser Cys Pro Glu Val Lys Val Phe Glu Asp Ile Ser Ala		
	565	570	575
	Asn Thr Val Asn Met Ala Leu Gln Ile Pro Gln Tyr Phe Leu Leu Thr		
	580	585	590
	Cys Gly Glu Val Val Phe Ser Val Thr Gly Leu Glu Phe Ser Tyr Ser		
20	595	600	605
	Gln Ala Pro Ser Asn Met Lys Ser Val Leu Gln Ala Gly Trp Leu Leu		
	610	615	620
	Thr Val Ala Val Gly Asn Ile Ile Val Leu Ile Val Ala Gly Ala Gly		
	625	630	635
	Gln Phe Ser Lys Gln Trp Ala Glu Tyr Ile Leu Phe Ala Ala Leu Leu		
	645	650	655
	Leu Val Val Cys Val Val Phe Ala Ile Met Ala Arg Phe Tyr Thr Tyr		
	660	665	670
25	Ile Asn Pro Ala Glu Ile Glu Ala Gln Phe Asp Glu Asp Glu Lys Lys		
	675	680	685
	Asn Arg Leu Glu Lys Ser Asn Pro Tyr Phe Met Ser Gly Ala Asn Ser		
	690	695	700
	Gln Lys Gln Met		
	705		

## (2) INFORMATION FOR SEQ ID NO:177:

30 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 3345 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA  
 (ix) FEATURE:

35 (A) NAME/KEY: Coding Sequence  
 (B) LOCATION: 88...2583  
 (D) OTHER INFORMATION:

CAC CAG ACT GGG ATA CCC ACT GTG GGC ATG GCA GTT GGT ATA CTG CTG His Gln Thr Gly Ile Pro Thr Val Gly Met Ala Val Gly Ile Leu Leu 780 785 790	2466
ACC ACC CTT CTG GTG ATT GGT ATA ATT TTA GCA GTT GTG TTT ATC CGC Thr Thr Leu Leu Val Ile Gly Ile Ile Leu Ala Val Val Phe Ile Arg 795 800 805	2514
5 ATA AAG AAG GAT AAA CGC AAA GAT AAT GTT GAA AGT CCT CAA GCA TCT Ile Lys Lys Asp Lys Gly Lys Asp Asn Val Glu Ser Ala Gln Ala Ser 810 815 820 825	2562
GAA GTC AAA CCT CTG AGA AGC TGAATTTGAA AAGGAATGTT TGAATTTATA TAGC Glu Val Lys Pro Leu Arg Ser 830	2617
10 AAGTGCTATT TCAGCAACAA CCATCTCATC CTATTACTTT TCATCTAACG TGCATTATAA TTTTTAAAC AGATATTCCC TCTTGTCCCT TAATATTTGC TAAATATTTC TTTTTTGAGG TGGAGTCTTG CTCTGTCGCC CAGGCTGGAG TACAGTGGTG TGATCCCAGC TCACTGCAAC CTCCGCCTCC TGGGTTCACA TGATTCTCT GCCTCAGCTT CCTAAGTAGC TGGGTTTACA GGCACCCACC ACCATGCCCA GCTAATTTT GTATTTTAA TAGAGACGGG GTTTCGCCAT TTGGCCAGGC TGGTCTTGAA CTCCCTGACGT CAAGTGATCT GCCTGCCTTG GTCTCCCAAT ACAGGCATGA ACCACTGCAC CCACCTACTT AGATATTTCA TGTGCTATAG ACATTAGAGA GATTTTCAT TTTTCCATGA CATTTCCTCT CTCTGCAAAT GGCTTAGCTA CTTGTGTTTT 15 TCCCTTTGG GGCAAGACAG ACTCATTAAA TATTCTGTAC ATTTTTTCTT TATCAAGGAG ATATATCAGT GTTGTCCTCAT AGAACTGCTT GGATTCCATT TATGTTTTTT CTGATTCCAT CCTGTGTCCC CTTCATCCTT GACTCCTTIG GTATTTCACT GAATTTCAAA CATTITGTCAG AGAAGAAAAA AGTGAGGACT CAGGAAAAAT AAATAAATAA AAGAACAGCC TTTTGCAGGCC GCGAATTG	2677 2737 2797 2857 2917 2977 3037 3097 3157 3217 3277 3337 3345

## (2) INFORMATION FOR SEQ ID NO:178:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 832 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS:
  - (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:

Met Ile Leu Gln Ala His Leu His Ser Leu Cys Leu Leu Met Leu Tyr 25 1 5 10 15
Leu Ala Thr Gly Tyr Gly Gln Glu Gly Lys Phe Ser Gly Pro Leu Lys 20 25 30
Pro Met Thr Phe Ser Ile Tyr Glu Gly Gln Glu Pro Ser Gln Ile Ile 35 40 45
Phe Gln Phe Lys Ala Asn Pro Pro Ala Val Thr Phe Glu Leu Thr Gly 50 55 60
Glu Thr Asp Asn Ile Phe Val Ile Glu Arg Glu Gly Leu Leu Tyr Tyr 65 70 75 80
Asn Arg Ala Leu Asp Arg Glu Thr Arg Ser Thr His Asn Leu Gln Val 80 85 90 95
Ala Ala Leu Asp Ala Asn Gly Ile Ile Val Glu Gly Pro Val Pro Ile 100 105 110
Thr Ile Glu Val Lys Asp Ile Asn Asp Asn Arg Pro Thr Phe Leu Gln 115 120 125
Ser Lys Tyr Glu Gly Ser Val Arg Gln Asn Ser Arg Pro Gly Lys Pro 130 135 140
Phe Leu Tyr Val Asn Ala Thr Asp Leu Asp Asp Pro Ala Thr Pro Asn 145 150 155 160
Gly Gln Leu Tyr Tyr Gln Ile Val Ile Gln Leu Pro Met Ile Asn Asn 165 170 175
Val Met Tyr Phe Gln Ile Asn Asn Lys Thr Gly Ala Ile Ser Leu Thr 180 185 190

Arg Glu Gly Ser Gln Glu Leu Asn Pro Ala Lys Asn Pro Ser Tyr Asn  
 195 200 205  
 Leu Val Ile Ser Val Lys Asp Met Gly Gly Gln Ser Glu Asn Ser Phe  
 210 215 220  
 Ser Asp Thr Thr Ser Val Asp Ile Ile Val Thr Glu Asn Ile Trp Lys  
 225 230 235 240  
 Ala Pro Lys Pro Val Glu Met Val Glu Asn Ser Thr Asp Pro His Pro  
 245 250 255  
 5 Ile Lys Ile Thr Gln Val Arg Trp Asn Asp Pro Gly Ala Gln Tyr Ser  
 260 265 270  
 Leu Val Asp Lys Glu Lys Leu Pro Arg Phe Pro Phe Ser Ile Asp Gln  
 275 280 285  
 Glu Gly Asp Ile Tyr Val Thr Gln Pro Leu Asp Arg Glu Glu Lys Asp  
 290 295 300  
 Ala Tyr Val Phe Tyr Ala Val Ala Lys Asp Glu Tyr Gly Lys Pro Leu  
 305 310 315 320  
 10 Ser Tyr Pro Leu Glu Ile His Val Lys Val Lys Asp Ile Asn Asp Asn  
 325 330 335  
 Pro Pro Thr Cys Pro Ser Pro Val Thr Val Phe Glu Val Gln Glu Asn  
 340 345 350  
 Glu Arg Leu Gly Asn Ser Ile Gly Thr Leu Thr Ala His Asp Arg Asp  
 355 360 365  
 Glu Glu Asn Thr Ala Asn Ser Phe Leu Asn Tyr Arg Ile Val Glu Gln  
 370 375 380  
 Thr Pro Lys Leu Pro Met Asp Gly Leu Phe Leu Ile Gln Thr Tyr Ala  
 385 390 395 400  
 15 Gly Met Leu Gln Leu Ala Lys Gln Ser Leu Lys Lys Gln Asp Thr Pro  
 405 410 415  
 Gln Tyr Asn Leu Thr Ile Glu Val Ser Asp Lys Asp Phe Lys Thr Leu  
 420 425 430  
 Cys Phe Val Gln Ile Asn Val Ile Asp Ile Asn Asp Gln Ile Pro Ile  
 435 440 445  
 Phe Glu Lys Ser Asp Tyr Gly Asn Leu Thr Leu Ala Glu Asp Thr Asn  
 450 455 460  
 20 Ile Gly Ser Thr Ile Leu Thr Ile Gln Ala Thr Asp Ala Asp Glu Pro  
 465 470 475 480  
 Phe Thr Gly Ser Ser Lys Ile Leu Tyr His Ile Ile Lys Gly Asp Ser  
 485 490 495  
 Glu Gly Arg Leu Gly Val Asp Thr Asp Pro His Thr Asn Thr Gly Tyr  
 500 505 510  
 Val Ile Ile Lys Lys Pro Leu Asp Phe Glu Thr Ala Ala Val Ser Asn  
 515 520 525  
 25 Ile Val Phe Lys Ala Glu Asn Pro Glu Pro Leu Val Phe Gly Val Lys  
 530 535 540  
 Tyr Asn Ala Ser Ser Phe Ala Lys Phe Thr Leu Ile Val Thr Asp Val  
 545 550 555 560  
 Asn Glu Ala Pro Gln Phe Ser Gln His Val Phe Gln Ala Lys Val Ser  
 565 570 575  
 Glu Asp Val Ala Ile Gly Thr Lys Val Gly Asn Val Thr Ala Lys Asp  
 580 585 590  
 Pro Glu Gly Leu Asp Ile Ser Tyr Ser Leu Arg Gly Asp Thr Arg Gly  
 595 600 605  
 30 Trp Leu Lys Ile Asp His Val Thr Gly Glu Ile Phe Ser Val Ala Pro  
 610 615 620  
 Leu Asp Arg Glu Ala Gly Ser Pro Tyr Arg Val Gln Val Val Ala Thr  
 625 630 635 640  
 Glu Val Gly Gly Ser Ser Leu Ser Ser Val Ser Glu Phe His Leu Ile  
 645 650 655  
 Leu Met Asp Val Asn Asp Asn Pro Pro Arg Leu Ala Lys Asp Tyr Thr  
 660 665 670  
 Gly Leu Phe Phe Cys His Pro Leu Ser Ala Pro Gly Ser Leu Ile Phe  
 675 680 685  
 35 Glu Ala Thr Asp Asp Asp Gln His Leu Phe Arg Gly Pro His Phe Thr  
 690 695 700  
 Phe Ser Leu Gly Ser Gly Ser Leu Gln Asn Asp Trp Glu Val Ser Lys  
 705 710 715 720

Ile Asn Gly Thr His Ala Arg Leu Ser Thr Arg His Thr Asp Phe Glu  
 725 730 735  
 Glu Arg Ala Tyr Val Val Leu Ile Arg Ile Asn Asp Gly Gly Arg Pro  
 740 745 750  
 Pro Leu Glu Gly Ile Val Ser Leu Pro Val Thr Phe Cys Ser Cys Val  
 755 760 765  
 Glu Gly Ser Cys Phe Arg Pro Ala Gly His Gln Thr Gly Ile Pro Thr  
 770 775 780  
 5 Val Gly Met Ala Val Gly Ile Leu Leu Thr Thr Leu Leu Val Ile Gly  
 785 790 795 800  
 Ile Ile Leu Ala Val Val Phe Ile Arg Ile Lys Lys Asp Lys Gly Lys  
 805 810 815  
 Asp Asn Val Glu Ser Ala Gln Ala Ser Glu Val Lys Pro Leu Arg Ser  
 820 825 830

## (2) INFORMATION FOR SEQ ID NO:179:

10 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1827 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:

Met Ala Arg Lys Lys Phe Ser Gly Leu Glu Ile Ser Leu Ile Val Leu  
 1 5 10 15  
 Phe Val Ile Val Thr Ile Ile Ala Ile Ala Leu Ile Val Val Leu Ala  
 20 25 30  
 Thr Lys Thr Pro Ala Val Asp Glu Ile Ser Asp Ser Thr Ser Thr Pro  
 35 40 45  
 Ala Thr Thr Arg Val Thr Thr Asn Pro Ser Asp Ser Gly Lys Cys Pro  
 50 55 60  
 20 Asn Val Leu Asn Asp Pro Val Asn Val Arg Ile Asn Cys Ile Pro Glu  
 65 70 75 80  
 Gln Phe Pro Thr Glu Gly Ile Cys Ala Gln Arg Gly Cys Cys Trp Arg  
 85 90 95  
 Pro Trp Asn Asp Ser Leu Ile Pro Trp Cys Phe Phe Val Asp Asn His  
 100 105 110  
 Gly Tyr Asn Val Gln Asp Met Thr Thr Ser Ile Gly Val Glu Ala  
 115 120 125  
 25 Lys Leu Asn Arg Ile Pro Ser Pro Thr Leu Phe Gly Asn Asp Ile Asn  
 130 135 140  
 Ser Val Leu Phe Thr Thr Gln Asn Gln Thr Pro Asn Arg Phe Arg Phe  
 145 150 155 160  
 Lys Ile Thr Asp Pro Asn Asn Arg Arg Tyr Glu Val Pro His Gln Tyr  
 165 170 175  
 Val Lys Glu Phe Thr Gly Pro Thr Val Ser Asp Thr Leu Tyr Asp Val  
 180 185 190  
 Lys Val Ala Gln Asn Pro Phe Ser Ile Gln Val Ile Arg Lys Ser Asn  
 195 200 205  
 30 Gly Lys Thr Leu Phe Asp Thr Ser Ile Gly Pro Leu Val Tyr Ser Asp  
 210 215 220  
 Gln Tyr Leu Gln Ile Ser Ala Arg Leu Pro Ser Asp Tyr Ile Tyr Gly  
 225 230 235 240  
 Ile Gly Glu Gln Val His Lys Arg Phe Arg His Asp Leu Ser Trp Lys  
 245 250 255  
 Thr Trp Pro Ile Phe Thr Arg Asp Gln Leu Pro Gly Asp Asn Asn Asn  
 260 265 270  
 35 Asn Leu Tyr Gly His Gln Thr Phe Phe Met Cys Ile Glu Asp Thr Ser  
 275 280 285  
 Gly Lys Ser Phe Gly Val Phe Leu Met Asn Ser Asn Ala Met Glu Ile  
 290 295 300  
 Phe Ile Gln Pro Thr Pro Ile Val Thr Tyr Arg Val Thr Gly Gly Ile

305	310	315	320
Leu Asp Phe Tyr Ile Leu Leu Gly Asp Thr Pro Glu Gln Val Val Gln			
325	330	335	
Gln Tyr Gln Gln Leu Val Gly Leu Pro Ala Met Pro Ala Tyr Trp Asn			
340	345	350	
Leu Gly Phe Gln Leu Ser Arg Trp Asn Tyr Lys Ser Leu Asp Val Val			
355	360	365	
5 Lys Glu Val Val Arg Arg Asn Arg Glu Ala Gly Ile Pro Phe Asp Thr			
370	375	380	
Gln Val Thr Asp Ile Asp Tyr Met Glu Asp Lys Lys Asp Phe Thr Tyr			
385	390	395	400
Asp Gln Val Ala Phe Asn Gly Leu Pro Gln Phe Val Gln Asp Leu His			
405	410	415	
Asp His Gly Gln Lys Tyr Val Ile Ile Leu Asp Pro Ala Ile Ser Ile			
420	425	430	
Gly Arg Arg Ala Asn Gly Thr Thr Tyr Ala Thr Tyr Glu Arg Gly Asn			
435	440	445	
10 Thr Gln His Val Trp Ile Asn Glu Ser Asp Gly Ser Thr Pro Ile Ile			
450	455	460	
Gly Glu Val Trp Pro Gly Leu Thr Val Tyr Pro Asp Phe Thr Asn Pro			
465	470	475	480
Asn Cys Ile Asp Trp Trp Ala Asn Glu Cys Ser Ile Phe His Gln Glu			
485	490	495	
Val Gln Tyr Asp Gly Leu Trp Ile Asp Met Asn Glu Val Ser Ser Phe			
500	505	510	
15 Ile Gln Gly Ser Thr Lys Gly Cys Asn Val Asn Lys Leu Asn Tyr Pro			
515	520	525	
Pro Phe Thr Pro Asp Ile Leu Asp Lys Leu Met Tyr Ser Lys Thr Ile			
530	535	540	
Cys Met Asp Ala Val Gln Asn Trp Gly Lys Gln Tyr Asp Val His Ser			
545	550	555	560
Leu Tyr Gly Tyr Ser Met Ala Ile Ala Thr Glu Gln Ala Val Gln Lys			
565	570	575	
Val Phe Pro Asn Lys Arg Ser Phe Ile Leu Thr Arg Ser Thr Phe Ala			
580	585	590	
20 Gly Ser Gly Arg His Ala Ala His Trp Leu Gly Asp Asn Thr Ala Ser			
595	600	605	
Trp Glu Gln Met Glu Trp Ser Ile Thr Gly Met Leu Glu Phe Ser Leu			
610	615	620	
Phe Gly Ile Pro Leu Val Gly Ala Asp Ile Cys Gly Phe Val Ala Glu			
625	630	635	640
Thr Thr Glu Glu Leu Cys Arg Arg Trp Met Gln Leu Gly Ala Phe Tyr			
645	650	655	
25 Pro Phe Ser Arg Asn His Asn Ser Asp Gly Tyr Glu His Gln Asp Pro			
660	665	670	
Ala Phe Phe Gly Gln Asn Ser Leu Leu Val Lys Ser Ser Arg Gln Tyr			
675	680	685	
Leu Thr Ile Arg Tyr Thr Leu Leu Pro Phe Leu Tyr Thr Leu Phe Tyr			
690	695	700	
Lys Ala His Val Phe Gly Glu Thr Val Ala Arg Pro Val Leu His Glu			
705	710	715	720
Phe Tyr Glu Asp Thr Asn Ser Trp Ile Glu Asp Thr Glu Phe Leu Trp			
725	730	735	
30 Gly Pro Ala Leu Leu Ile Thr Pro Val Leu Lys Gln Gly Ala Asp Thr			
740	745	750	
Val Ser Ala Tyr Ile Pro Asp Ala Ile Trp Tyr Asp Tyr Glu Ser Gly			
755	760	765	
Ala Lys Arg Pro Trp Arg Lys Gln Arg Val Asp Met Tyr Leu Pro Ala			
770	775	780	
Asp Lys Ile Gly Leu His Leu Arg Gly Gly Tyr Ile Ile Pro Ile Gln			
785	790	795	800
35 Glu Pro Asp Val Thr Thr Ala Ser Arg Lys Asn Pro Leu Gly Leu			
805	810	815	
Ile Val Ala Leu Gly Glu Asn Asn Thr Ala Lys Gly Asp Phe Phe Trp			
820	825	830	
Asp Asp Gly Glu Thr Lys Asp Thr Ile Gln Asn Gly Asn Tyr Ile Leu			

	835	840	845
	Tyr Thr Phe Ser Val Ser Asn Asn Thr Leu Asp Ile Val Cys Thr His		
	850	855	860
	Ser Ser Tyr Gln Glu Gly Thr Thr Leu Ala Phe Gln Thr Val Lys Ile		
	865	870	875
	Leu Gly Leu Thr Asp Ser Val Thr Glu Val Arg Val Ala Glu Asn Asn		880
	885	890	895
5	Gln Pro Met Asn Ala His Ser Asn Phe Thr Tyr Asp Ala Ser Asn Gln		
	900	905	910
	Val Leu Leu Ile Ala Asp Leu Lys Leu Asn Leu Gly Arg Asn Phe Ser		
	915	920	925
	Val Gln Trp Asn Gln Ile Phe Ser Glu Asn Glu Arg Phe Asn Cys Tyr		
	930	935	940
	Pro Asp Ala Asp Leu Ala Thr Glu Gln Lys Cys Thr Gln Arg Gly Cys		
	945	950	955
	Val Trp Arg Thr Gly Ser Ser Leu Ser Lys Ala Pro Glu Cys Tyr Phe		960
	965	970	975
10	Pro Arg Gln Asp Asn Ser Tyr Ser Val Asn Ser Ala Arg Tyr Ser Ser		
	980	985	990
	Met Gly Ile Thr Ala Asp Leu Gln Leu Asn Thr Ala Asn Ala Arg Ile		
	995	1000	1005
	Lys Leu Pro Ser Asp Pro Ile Ser Thr Leu Arg Val Glu Val Lys Tyr		
	1010	1015	1020
	His Lys Asn Asp Met Leu Gln Phe Lys Ile Tyr Asp Pro Gln Lys Lys		
	025	1030	1035
	Arg Tyr Glu Val Pro Val Pro Leu Asn Ile Pro Thr Thr Pro Ile Ser		1040
	1045	1050	1055
	Thr Tyr Glu Asp Arg Leu Tyr Asp Val Glu Ile Lys Glu Asn Pro Phe		
	1060	1065	1070
	Gly Ile Gln Ile Arg Arg Ser Ser Gly Arg Val Ile Trp Asp Ser		
	1075	1080	1085
	Trp Leu Pro Gly Phe Ala Phe Asn Asp Gln Phe Ile Gln Ile Ser Thr		
	1090	1095	1100
	Arg Leu Pro Ser Glu Tyr Ile Tyr Gly Phe Gly Glu Val Glu His Thr		
	105	1110	1115
	Ala Phe Lys Arg Asp Leu Asn Trp Asn Thr Trp Gly Met Phe Thr Arg		1120
	1125	1130	1135
	Asp Gln Pro Pro Gly Tyr Lys Leu Asn Ser Tyr Gly Phe His Pro Tyr		
	1140	1145	1150
	Tyr Met Ala Leu Glu Glu Gly Asn Ala His Gly Val Phe Leu Leu		
	1155	1160	1165
	Asn Ser Asn Ala Met Asp Val Thr Phe Gln Pro Thr Pro Ala Leu Thr		
	1170	1175	1180
20	Tyr Arg Thr Val Gly Gly Ile Leu Asp Phe Tyr Met Phe Leu Gly Pro		
	185	1190	1195
	Thr Pro Gln Val Ala Thr Lys Gln Tyr His Glu Val Ile Gly His Pro		1200
	1205	1210	1215
	Val Met Pro Ala Tyr Trp Ala Leu Gly Phe Gln Leu Cys Arg Tyr Gly		
	1220	1225	1230
	Tyr Ala Asn Thr Ser Glu Val Arg Glu Leu Tyr Asp Ala Met Val Ala		
	1235	1240	1245
	Ala Asn Ile Pro Tyr Asp Val Gln Tyr Thr Asp Ile Asp Tyr Met Glu		
	1250	1255	1260
25	Arg Gln Leu Asp Phe Thr Ile Gly Glu Ala Phe Gln Asp Leu Pro Gln		
	265	1270	1275
	Phe Val Asp Lys Ile Arg Gly Glu Met Arg Tyr Ile Ile Leu		1280
	1285	1290	1295
	Asp Pro Ala Ile Ser Gly Asn Glu Thr Lys Thr Tyr Pro Ala Phe Glu		
	1300	1305	1310
	Arg Gly Gln Gln Asn Asp Val Phe Val Lys Trp Pro Asn Thr Asn Asp		
	1315	1320	1325
30	Ile Cys Trp Ala Lys Val Trp Pro Asp Leu Pro Asn Ile Thr Ile Asp		
	1330	1335	1340
	Lys Thr Leu Thr Glu Asp Glu Ala Val Asn Ala Ser Arg Ala His Val		
	345	1350	1355
	Ala Phe Pro Asp Phe Phe Arg Thr Ser Thr Ala Glu Trp Trp Ala Arg		1360

	1365	1370	1375	
	Glu Ile Val Asp Phe Tyr Asn Glu Lys Met Lys Phe Asp Gly Leu Trp			
	1380	1385	1390	
	Ile Asp Met Asn Glu Pro Ser Ser Phe Val Asn Gly Thr Thr Thr Asn			
	1395	1400	1405	
	Gln Cys Arg Asn Asp Glu Leu Asn Tyr Pro Pro Tyr Phe Pro Glu Leu			
	1410	1415	1420	
5	Thr Lys Arg Thr Asp Gly Leu His Phe Arg Thr Ile Cys Met Glu Ala			
	425	1430	1435	1440
	Glu Gln Ile Leu Ser Asp Gly Thr Ser Val Leu His Tyr Asp Val His			
	1445	1450	1455	
	Asn Leu Tyr Gly Trp Ser Gln Met Lys Pro Thr His Asp Ala Leu Gln			
	1460	1465	1470	
	Lys Thr Thr Gly Lys Arg Gly Ile Val Ile Ser Arg Ser Thr Tyr Pro			
	1475	1480	1485	
	Thr Ser Gly Arg Trp Gly Gly His Trp Leu Gly Asp Asn Tyr Ala Arg			
	1490	1495	1500	
10	Trp Asp Asn Met Asp Lys Ser Ile Ile Gly Met Met Glu Phe Ser Leu			
	505	1510	1515	1520
	Phe Gly Ile Ser Tyr Thr Gly Ala Asp Ile Cys Gly Phe Phe Asn Asn			
	1525	1530	1535	
	Ser Glu Tyr His Leu Cys Thr Arg Trp Met Gln Leu Gly Ala Phe Tyr			
	1540	1545	1550	
	Pro Tyr Ser Arg Asn His Asn Ile Ala Asn Thr Arg Arg Gln Asp Pro			
	1555	1560	1565	
15	Ala Ser Trp Asn Glu Thr Phe Ala Glu Met Ser Arg Asn Ile Leu Asn			
	1570	1575	1580	
	Ile Arg Tyr Thr Leu Leu Pro Tyr Phe Tyr Thr Gln Met His Glu Ile			
	585	1590	1595	1600
	His Ala Asn Gly Gly Thr Val Ile Arg Pro Leu Leu His Glu Phe Phe			
	1605	1610	1615	
	Asp Glu Lys Pro Thr Trp Asp Ile Phe Lys Gln Phe Leu Trp Gly Pro			
	1620	1625	1630	
	Ala Phe Met Val Thr Pro Val Leu Glu Pro Tyr Val Gln Thr Val Asn			
20	1635	1640	1645	
	Ala Tyr Val Pro Asn Ala Arg Trp Phe Asp Tyr His Thr Gly Lys Asp			
	1650	1655	1660	
	Ile Gly Val Arg Gly Gln Phe Gln Thr Phe Asn Ala Ser Tyr Asp Thr			
	665	1670	1675	1680
	Ile Asn Leu His Val Arg Gly Gly His Ile Leu Pro Cys Gln Glu Pro			
	1685	1690	1695	
	Ala Gln Asn Thr Phe Tyr Ser Arg Gln Lys His Met Lys Leu Ile Val			
	1700	1705	1710	
25	Ala Ala Asp Asp Asn Gln Met Ala Gln Gly Ser Leu Phe Trp Asp Asp			
	1715	1720	1725	
	Gly Glu Ser Ile Asp Thr Tyr Glu Arg Asp Leu Tyr Leu Ser Val Gln			
	1730	1735	1740	
	Phe Asn Leu Asn Gln Thr Thr Leu Thr Ser Thr Ile Leu Lys Arg Gly			
	745	1750	1755	1760
	Tyr Ile Asn Lys Ser Glu Thr Arg Leu Gly Ser Leu His Val Trp Gly			
	1765	1770	1775	
	Lys Gly Thr Thr Pro Val Asn Ala Val Thr Leu Thr Tyr Asn Gly Asn			
30	1780	1785	1790	
	Lys Asn Ser Leu Pro Phe Asn Glu Asp Thr Thr Asn Met Ile Leu Arg			
	1795	1800	1805	
	Ile Asp Leu Thr Thr His Asn Val Thr Leu Glu Glu Pro Ile Glu Ile			
	1810	1815	1820	
	Asn Trp Ser			
	825			

## (2) INFORMATION FOR SEQ ID NO:180:

35

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 2284 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single

B

	CTT TTC ACA CTC CCT GGA ACT CCT ATA ACT TAC TAT GGA GAA GAA ATT Leu Phe Thr Leu Pro Gly Thr Pro Ile Thr Tyr Tyr Gly Glu Glu Ile 470 475 480	1496
	GGA ATG GGA AAT ATT GTA GCC GCA AAT CTC AAT GAA AGC TAT GAT ATT Gly Met Gly Asn Ile Val Ala Ala Asn Leu Asn Glu Ser Tyr Asp Ile 485 490 495 500	1544
5	AAT ACC CTT CGC TCA AAG TCA CCA ATG CAG TGG GAC AAT AGT TCA AAT Asn Thr Leu Arg Ser Lys Ser Pro Met Gln Trp Asp Asn Ser Ser Asn 505 510 515	1592
	GCT GGT TTT TCT GAA GCT AGT AAC ACC TGG TTA CCT ACC AAT TCA GAT Ala Gly Phe Ser Glu Ala Ser Asn Thr Trp Leu Pro Thr Asn Ser Asp 520 525 530	1640
10	TAC CAC ACT GTG AAT GTT GAT GTC CAA AAG ACT CAG CCC AGA TCG GCT Tyr His Thr Val Asn Val Asp Val Gln Lys Thr Gln Pro Arg Ser Ala 535 540 545	1688
	TTG AAG TTA TAT CAA GAT TTA AGT CTA CTT CAT GCC AAT GAG CTA CTC Leu Lys Leu Tyr Gln Asp Leu Ser Leu Leu His Asn Glu Leu Leu 550 555 560	1736
15	CTC AAC AGG GGC TGG TTT TGC CAT TTG AGG AAT GAC AGC CAC TAT GTT Leu Asn Arg Gly Trp Phe Cys His Leu Arg Asn Asp Ser His Tyr Val 565 570 575 580	1784
	GTG TAC ACA AGA GAG CTG GAT GGC ATC GAC AGA ATC TTT ATC GTG GTT Val Tyr Thr Arg Glu Leu Asp Gly Ile Asp Arg Ile Phe Ile Val Val 585 590 595	1832
20	CTG AAT TTT GGA GAA TCA ACA CTG TTA AAT CTA CAT AAT ATG ATT TCG Leu Asn Phe Gly Glu Ser Thr Leu Leu Asn Leu His Asn Met Ile Ser 600 605 610	1880
	GGC CTT CCC GCT AAA ATA AGA ATA AGG TTA AGT ACC AAT TCT GCC GAC Gly Leu Pro Ala Lys Ile Arg Ile Arg Leu Ser Thr Asn Ser Ala Asp 615 620 625	1928
	AAA GGC AGT AAA GTT GAT ACA AGT GGC ATT TTT CTG GAC AAG GGA GAG Lys Gly Ser Lys Val Asp Thr Ser Gly Ile Phe Leu Asp Lys Gly Glu 630 635 640	1976
25	GGA CTC ATC TTT GAA CAC AAC ACG AAG AAT CTC CTT CAT CGC CAA ACA Gly Leu Ile Phe Glu His Asn Thr Lys Asn Leu Leu His Arg Gln Thr 645 650 655 660	2024
	GCT TTC AGA GAT AGA TGC TTT GTT TCC AAT CGA GCA TGC TAT TCC AGT Ala Phe Arg Asp Arg Cys Phe Val Ser Asn Arg Ala Cys Tyr Ser Ser 665 670 675	2072
30	GTA CTG AAC ATA CTG TAT ACC TCG TGT TAGGCACCTT TATGAAGAGA TGAAGAC Val Leu Asn Ile Leu Tyr Thr Ser Cys 680 685	2126
	ACTGGCATTT CAGTGGGATT GTAAGCATT GTAATAGCTT CATGTACAGC ATGCTGCTTG GTGAACAATC ATTAATTCTT CGATAATTCT GTAGCTTGAA TGAAACCGCT TTAAGAAAGG TTCTCAAATG TTTTAAAAAA AATAAAATGT TTAAAAGT	2186 2246 2284

## (2) INFORMATION FOR SEQ ID NO:181:

35 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 685 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:

	Met	Ala	Glu	Asp	Lys	Ser	Lys	Arg	Asp	Ser	Ile	Glu	Met	Ser	Met	Lys	
5	1				5				10				15				
	Gly	Cys	Gln	Thr	Asn	Asn	Gly	Phe	Val	His	Asn	Glu	Asp	Ile	Leu	Glu	
					20				25				30				
	Gln	Thr	Pro	Asp	Pro	Gly	Ser	Ser	Thr	Asp	Asn	Leu	Lys	His	Ser	Thr	
					35				40				45				
	Arg	Gly	Ile	Leu	Gly	Ser	Gln	Glu	Pro	Asp	Phe	Lys	Gly	Val	Gln	Pro	
					50				55				60				
	Tyr	Ala	Gly	Met	Pro	Lys	Glu	Val	Leu	Phe	Gln	Phe	Ser	Gly	Gln	Ala	
					65				70				75			80	
10	Arg	Tyr	Arg	Ile	Pro	Arg	Glu	Ile	Leu	Phe	Trp	Leu	Thr	Val	Ala	Ser	
					85				90				95				
	Val	Leu	Val	Leu	Ile	Ala	Ala	Thr	Ile	Ala	Ile	Ala	Leu	Ser	Pro		
					100				105				110				
	Lys	Cys	Leu	Asp	Trp	Trp	Gln	Glu	Gly	Pro	Met	Tyr	Gln	Ile	Tyr	Pro	
					115				120				125				
	Arg	Ser	Phe	Lys	Asp	Ser	Asn	Lys	Asp	Gly	Asn	Gly	Asp	Leu	Lys	Gly	
					130				135				140				
	Ile	Gln	Asp	Lys	Leu	Asp	Tyr	Ile	Thr	Ala	Leu	Asn	Ile	Lys	Thr	Val	
					145				150				155			160	
15	Trp	Ile	Thr	Ser	Phe	Tyr	Lys	Ser	Ser	Leu	Lys	Asp	Phe	Arg	Tyr	Gly	
					165				170				175				
	Val	Glu	Asp	Phe	Arg	Glu	Val	Asp	Pro	Ile	Phe	Gly	Thr	Met	Glu	Asp	
					180				185				190				
	Phe	Glu	Asn	Leu	Val	Ala	Ala	Ile	His	Asp	Lys	Gly	Leu	Lys	Leu	Ile	
					195				200				205				
	Ile	Asp	Phe	Ile	Pro	Asn	His	Thr	Ser	Asp	Lys	His	Ile	Trp	Phe	Gln	
					210				215				220				
20	Leu	Ser	Arg	Thr	Arg	Thr	Gly	Lys	Tyr	Thr	Asp	Tyr	Tyr	Ile	Trp	His	
					225				230				235			240	
	Asp	Cys	Thr	His	Glu	Asn	Gly	Lys	Thr	Ile	Pro	Pro	Asn	Asn	Trp	Leu	
					245				250				255				
	Ser	Val	Tyr	Gly	Asn	Ser	Ser	Trp	His	Phe	Asp	Glu	Val	Arg	Asn	Gln	
					260				265				270				
	Cys	Tyr	Phe	His	Gln	Phe	Met	Lys	Glu	Gln	Pro	Asp	Leu	Asn	Phe	Arg	
					275				280				285				
	Asn	Pro	Asp	Val	Gln	Glu	Glu	Ile	Lys	Glu	Ile	Leu	Arg	Phe	Trp	Leu	
					290				295				300				
25	Thr	Lys	Gly	Val	Asp	Gly	Phe	Ser	Leu	Asp	Ala	Val	Lys	Phe	Leu	Leu	
					305				310				315			320	
	Glu	Ala	Lys	His	Leu	Arg	Asp	Glu	Ile	Gln	Val	Asn	Lys	Thr	Gln	Ile	
					325				330				335				
	Pro	Asp	Thr	Val	Thr	Gln	Tyr	Ser	Glu	Leu	Tyr	His	Asp	Phe	Thr	Thr	
					340				345				350				
	Thr	Gln	Val	Gly	Met	His	Asp	Ile	Val	Arg	Ser	Phe	Arg	Gln	Thr	Met	
					355				360				365				
30	Asp	Gln	Tyr	Ser	Thr	Glu	Pro	Gly	Arg	Tyr	Arg	Phe	Met	Gly	Thr	Glu	
					370				375				380				
	Ala	Tyr	Ala	Glu	Ser	Ile	Asp	Arg	Thr	Val	Met	Tyr	Tyr	Gly	Leu	Pro	
					385				390				395			400	
	Phe	Ile	Gln	Glu	Ala	Asp	Phe	Pro	Phe	Asn	Asn	Tyr	Leu	Ser	Met	Leu	
					405				410				415				
	Asp	Thr	Val	Ser	Gly	Asn	Ser	Val	Tyr	Glu	Val	Ile	Thr	Ser	Trp	Met	
					420				425				430				
	Glu	Asn	Met	Pro	Glu	Gly	Lys	Trp	Pro	Asn	Trp	Met	Ile	Gly	Gly	Pro	
					435				440				445				
35	Asp	Ser	Ser	Arg	Leu	Leu	Thr	Ser	Arg	Leu	Gly	Asn	Gln	Tyr	Val	Asn	Val
					450				455				460				
	Met	Asn	Met	Leu	Leu	Phe	Thr	Leu	Pro	Gly	Thr	Pro	Ile	Thr	Tyr	Tyr	
					465				470				475			480	

Gly Glu Glu Ile Gly Met Gly Asn Ile Val Ala Ala Asn Leu Asn Glu  
 485 490 495  
 Ser Tyr Asp Ile Asn Thr Leu Arg Ser Lys Ser Pro Met Gln Trp Asp  
 500 505 510  
 Asn Ser Ser Asn Ala Gly Phe Ser Glu Ala Ser Asn Thr Trp Leu Pro  
 515 520 525  
 Thr Asn Ser Asp Tyr His Thr Val Asn Val Asp Val Gln Lys Thr Gln  
 530 535 540  
 5 Pro Arg Ser Ala Leu Lys Leu Tyr Gln Asp Leu Ser Leu Leu His Ala  
 545 550 555 560  
 Asn Glu Leu Leu Leu Asn Arg Gly Trp Phe Cys His Leu Arg Asn Asp  
 565 570 575  
 Ser His Tyr Val Val Tyr Thr Arg Glu Leu Asp Gly Ile Asp Arg Ile  
 580 585 590  
 Phe Ile Val Val Leu Asn Phe Gly Glu Ser Thr Leu Leu Asn Leu His  
 595 600 605  
 10 Asn Met Ile Ser Gly Leu Pro Ala Lys Ile Arg Ile Arg Leu Ser Thr  
 610 615 620  
 Asn Ser Ala Asp Lys Gly Ser Lys Val Asp Thr Ser Gly Ile Phe Leu  
 625 630 635 640  
 Asp Lys Gly Glu Gly Leu Ile Phe Glu His Asn Thr Lys Asn Leu Leu  
 645 650 655  
 His Arg Gln Thr Ala Phe Arg Asp Arg Cys Phe Val Ser Asn Arg Ala  
 660 665 670  
 Cys Tyr Ser Ser Val Leu Asn Ile Leu Tyr Thr Ser Cys  
 675 680 685

15 (2) INFORMATION FOR SEQ ID NO:182:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 54 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: unknown

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:

Leu Val Pro Arg Gly Ser Pro Gly Ile Pro Gly Ser Arg Val Gly Gln  
 1 5 10 15  
 Cys Thr Asp Ser Asp Val Arg Arg Pro Trp Ala Arg Ser Cys Ala His  
 20 25 30  
 25 Gln Gly Cys Gly Ala Gly Thr Arg Asn Ser His Gly Cys Ile Thr Arg  
 35 40 45  
 Pro Leu Arg Gln Ala Ser  
 50

(2) INFORMATION FOR SEQ ID NO:183:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 19 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:183:

Ser Ala Arg Asp Ser Gly Pro Ala Glu Asp Gly Ser Arg Ala Val Arg  
 35 1 5 10 15  
 Leu Asn Gly

(2) INFORMATION FOR SEQ ID NO:184:

WHAT IS CLAIMED IS:

1. A purified protein which specifically binds to a gastro-intestinal tract receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI.

2. A protein which binds specifically to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:1-55 or a binding portion thereof.

3. A protein which binds specifically to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the amino acid sequence of the protein is selected from the group consisting of SEQ ID NOS:1-55, or a binding portion thereof.

4. The protein of claim 2 which comprises the amino acid sequence substantially as set forth in:  
SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 30, SEQ ID NO: 43, SEQ ID NO: 46, or SEQ ID NO: 52, or a binding portion thereof.

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5. The protein of claim 3, the amino acid sequence of which consists of the amino acid sequence substantially as set forth in: SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 30, SEQ ID NO: 43, SEQ ID NO: 46, or SEQ ID NO: 52, or a binding portion thereof.

6. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino

acid sequence of: Xaa<sub>1</sub> Thr Xaa<sub>2</sub> Xaa<sub>3</sub> Ser Xaa<sub>4</sub> Xaa<sub>5</sub> Xaa<sub>6</sub> Asn Xaa, Arg (SEQ ID NO:253), where Xaa<sub>1</sub> is Ser or Thr; Xaa<sub>2</sub> is Arg or Lys; Xaa<sub>3</sub> is Lys or Arg; Xaa<sub>4</sub> is Ser or Leu; Xaa<sub>5</sub> is Arg, Ile, Val, or Ser; Xaa<sub>6</sub> is Ser, Tyr, Phe, or His; and Xaa<sub>5</sub> is Pro, His or Arg.

7. The protein of claim 6 which is not more than 40 amino acids in length.

10 8. The protein of claim 6 which is not more than 30 amino acids in length.

9. The protein of claim 6 which is not more than 20 amino acids in length.

15 10. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, 20 positioned anywhere along its sequence, the contiguous amino acid sequence of: Asp Xaa<sub>1</sub> Asp Xaa<sub>2</sub> Arg Arg Xaa<sub>3</sub> Xaa<sub>4</sub> (SEQ ID NO:254) where Xaa<sub>1</sub> is Ser, Ala, or Gly; Xaa<sub>2</sub> is Val or Gln; Xaa<sub>3</sub> is Pro, Gly, or Ser; and Xaa<sub>4</sub> is Trp or Tyr.

25 11. The protein of claim 10 which is not more than 40 amino acids in length.

12. The protein of claim 10 which is not more than 30 amino acids in length.

30 13. The protein of claim 10 which is not more than 20 amino acids in length.

14. A protein of not more than 50 amino acids in 35 length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes,

positioned anywhere along its sequence, the contiguous amino acid sequence of: Val Arg Ser Gly Cys Gly Xaa<sub>1</sub> Xaa<sub>2</sub> Ser Ser (SEQ ID NO:255), where Xaa<sub>1</sub> is Ala or Phe; and Xaa<sub>2</sub> is Arg or His.

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15. The protein of claim 14 which is not more than 40 amino acids in length.

16. The protein of claim 14 which is not more than 10 30 amino acids in length.

17. The protein of claim 14 which is not more than 20 amino acids in length.

15 18. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino 20 acid sequence of: NTRKSSRSNPR (SEQ ID NO:256) or STKRSLIYNHR (SEQ ID NO:257) or STGRKVFNRR (SEQ ID NO:258) or TNAKHSSHNR (SEQ ID NO:259).

19. A protein of not more than 50 amino acids in 25 length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino acid sequence of: DSDVRRPW (SEQ ID NO:260) or AADQRRGW (SEQ 30 ID NO:261) or DGRGGRSY (SEQ ID NO:262).

20. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of 35 HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino

acid sequence of: RVRS (SEQ ID NO:263) or SVRSGCGFRGSS (SEQ ID NO:264) or SVRGCGAHSS (SEQ ID NO:265).

21. The protein of claim 1, 2, 3, 6, 10, 14, 18,  
5 19, or 20 which is purified.

22. A composition comprising the protein of claim  
1, 2, 3, 6, 10, 14, 18, 19, or 20, bound to a material  
comprising an active agent, said active agent being of value  
10 in the treatment of a mammalian disease or disorder.

23. The composition of claim 22 in which the  
active agent is a drug.

15 24. The composition of claim 22 in which the  
material is a particle containing the active agent.

25. The composition of claim 22 in which the  
material is a slow-release device containing the drug.

20 26. The composition of claim 22 in which the  
protein is covalently or noncovalently bound to the material.

27. A composition comprising a chimeric protein  
25 bound to a material comprising an active agent, in which the  
chimeric protein comprises a sequence selected from the group  
consisting of SEQ ID NOS:1-55 or a binding portion thereof  
fused via a covalent bond to an amino acid sequence of a  
second protein, in which the active agent is of value in the  
30 treatment of a mammalian disease or disorder.

28. A composition comprising the protein of claim  
1, 2, 3, 6, 10, 14, 18, 19, or 20 covalently bound to a  
particle containing a drug.

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29. A composition comprising the protein of claim  
1, 2, 3, 6, 10, 14, 18, 19, or 20 covalently bound to a drug.